

### **REMARKS**

Reconsideration of this application is respectfully requested.

Claims 238-297 and 299-238 are pending in the subject application. Claims 238-241, 264, 270-274, 304, 308-312, and 336-337 have been amended. No claims have been added or canceled. Accordingly, claims 238-297 and 299-238 as amended are presented for further prosecution on the merits.

Acknowledgment is made of the new group number to which this application has been assigned. Any and all future correspondence will be directed to Group Art Unit 1809.

Commensurate with their broad and complete disclosure, Applicants have effected above a number of amendments to the claims. These amendments affect claims 238-241, 264, 270-274, 304, 308-312, and 336-337. First, independent claims 238, 272 and 308 have been amended to recite that the labeled sugar moiety designated "SM" in the oligo- or polynucleotide (claim 238), the nucleotide (claim 272) and the composition (claim 308) is in fact a sugar moiety. Previously, these claims were limited to ribose and deoxyribose. Support for SM being a sugar moiety and not being limited to specific pentose sugars (ribose and deoxyribose) can be found in the original disclosure, for example, page 93, last paragraph, through page 94, first paragraph; page 96, first paragraph; and the originally filed claims (101 et seq.). In addition, Applicants would like to point out that allowance for the pending claims in related European Patent Application No. 88 10 4963.9 (EP 0 286 898 A2) is expected shortly in which "S" [originally "S" in the U.S. patent application but since then changed to "SM"] is claimed as a sugar moiety alone without limitation or clarification. Because of a backlog of applications in the European Patent Office, Applicants have not yet received the Communication Under Rule 51(4) EPC. As soon as this Communication is received, Applicants will submit a copy to the Examiner.

Besides changing the scope of protection sought in the main claims with respect to the sugar moiety (SM), Applicants have also taken the liberty of restricting the attachment of the variously recited elements, the phosphate moiety (PM), SM and the base moiety (BM) to covalent attachments.

The 2', 3' and 5' positions previously recited in claims 238, 272 and 308 have now been relegated to dependent claims. In this regard, claims 239, 273 and 309 have

each been amended to recite that Sig is attached to the C2' or the C3' or the C5' position of SM (the sugar moiety).

Another significant amendment is the inclusion of dideoxyribonucleotides in the presently claimed invention. "Dideoxyribonucleotide" is now recited in the alternative to "deoxyribonucleotide" in claims 240, 270, 274, 304, 310 and 336. Support for the term "dideoxyribonucleotide" is found in the original Ward disclosure, U.S. Patent Application Serial No. 06/255,223, filed on April 17, 1981, since then issued as U.S. Patent Nos. 4,711,955; 5,328,824; 5,449,767; and 5,476,928. The original Ward application was incorporated by reference in the present application by virtue of the statements given on page 2, last paragraph. For portions in U.S. Patent No. 4,711,955 that support the use of "dideoxyribonucleotide" in the present claims, see, for example, column 3, lines 21-66 (in particular, lines 56-60, "wherein x, y, and z represents H-, . . ."); column 7, lines 18-56 (in particular, lines 46-51, "wherein x, y and z represents H-, . . ."); and column 11, lines 30-35 ("wherein each of x, y, and z represents H-, . . ."). Claims have also issued in the foregoing Ward U.S. patents with subject matter directed to "dideoxyribonucleotide." Such an issued claim is the first claim in U.S. Patent No. 5,476,928 ("wherein each of x, y and z represents H-, . . ."). Finally, in addition to incorporating the Ward disclosure by reference on page 2 (last paragraph), Applicants wish to point out that a more specific reference was later made to the Ward disclosure in the present application, beginning on page 97, last paragraph, through page 98, first paragraph. There, Applicants disclosed:

The Sig component of the nucleotides in accordance with this invention and the nucleotides and polynucleotides incorporating the nucleotides of this invention containing the Sig component are equivalent to and useful for the same purposes as the nucleotides described in the above-identified U.S. patent application Serial No. 255,223. More specifically, the chemical moiety A described in U.S. patent application Serial No. 255,223 is functionally the equivalent of the Sig component or chemical moiety of the special nucleotides of this invention. Accordingly, the Sig component or chemical moiety of nucleotides of this invention can be directly covalently attached to the P, S or B moieties or attached thereto via a chemical linkage or linkage arm as described in U.S. patent application Ser. No. 255,223, as indicated by the dotted line connecting B and A of the nucleotides of U.S. Serial No. 255,223. The various linker arms or linkages identified in U.S. Ser. No. 255,223 are applicable to and useful in the preparation of the special nucleotides of this invention.

In order to provide a proper antecedent basis for recited language, claims 241 and 271 have been amended. The former claim refers to a ribonucleotide which is also recited now in the latter claim. Similar correspondence can now be found in claims 311

and 337, the latter depending from the former. Claim 337 previously depended from claim 309, but as now amended, it depends properly from claim 311.

Lastly, some wordsmithing changes have been made in the case of five claims. These include claim 241 ("An" changed to --The-- and "polyribonucleotide" changed to -polynucleotide--); claim 264 ("An" changed to --The--); and claims 310, 311 and 312 ("comprising" changed to --comprises--).

It is respectfully submitted that none of the foregoing amendments to the claims constitutes the insertion of new matter. Instead, all of the amendments represent subject matter to which Applicants are duly entitled to claim as part and parcel of their invention. Entry of all the amendments above is respectfully urged.

Applicants also appreciate the Examiner's remarks concerning the provisions of Public Law 103-465, effective June 8, 1995. Accordingly, this Amendment is accompanied by Applicants' Request Under 37 C.F.R. §1.129(a) For Withdrawal of The Finality Of The April 15, 1997 Office Action. A copy of Applicants' §1.129(a) Request is attached as Exhibit A. Because it is expected that the accompanying Request (Exhibit) will be granted, Applicants have taken the liberty of filing this Amendment under the provisions of 37 C.F.R. §1.115, and not §1.116, the latter being the statutorily prescribed form in response to a final rejection of the claims.

Before addressing the formal grounds of objection and rejection, Applicants would to take care of some housekeeping matters related to their September 11, 1995 Information Disclosure Statement. U.S. Patent Application Serial No. 255,223 cited on page 2 of Form PTO-1449 was not entered by the Examiner because it lacked a publication date. Actually, this application corresponds to Ward et al., U.S. Patent No. 4,711,955 that was cited on page 2 of Form PTO-1449, and accordingly, it need not be entered because to do so would create a duplicate entry. With respect to the three other publications, Koprinski et al. [J. Gen. Virol. 6:85 (1970)]; Bhat, [Syn. Proc. In Nucleic Acid Chem., Vol. I, p. 521 (1968)]; and Caruthers [Second Annual Congress for Recombinant DNA Research, Los Angeles, CA (1982)], cited on pages 1, 2 and 6, respectively, in the Forms PTO-1449, Applicants' undersigned attorney has obtained copies of all three publications. These three publications (Koprinski et al., Bhat and Caruthers) as well as their complete citations are listed on a new Form PTO-1449 attached to this Amendment as Exhibits B-E, respectively. It is respectfully requested that the Examiner consider these documents prior to issuing any formal indication of allowability in the instant application.

Turning now to the two substantive issues in the April 15, 1997 Office Action . . .

**The Objection and Rejection Under 35 U.S.C. §112, First Paragraph**

The specification stands objected to and claims 238, 240-272, 274-297, 299-308 and 310-338 were rejected for allegedly failing to adequately describe or enable the claimed invention. In the April 15, 1997 Office Action (pages 2 to 3), the Examiner stated that:

. . . the disclosure is enabling only for claims limited to "covalent" attachment of the Sig moiety to the sugar (SM) via hydroxyls at the 2', 3', or 5' positions. This is a relaxation of the previous rejection to include the 5' position labeling. The rejection is thus maintained from the previous office action, mailed 6/25/96, plus the above relaxation due to the persuasive arguments of applicants directed to 5' labeling. Also, the above rejection is necessitated by amendment regarding newly-added claims rejected due to their scope being beyond the enabled 2', 3', and 5' SM labeling positions. Applicants also argue that branched sugar nucleoside labeling as broadening the enabled scope. Consideration of this argument reveals that only 2' or 3' labeling is therein discussed which is stated above as being acknowledged as being enabled. RNA labeling is argued but is also acknowledged as instantly enabled due to 2' or 3' labeling. The poly-L-lysine labeling is also at the stated enabled positions on the SM moiety. The phosphate group labeling that is further argued, however, is deemed a PM-labeling type that is outside the scope of the instant claims and therefore moot regarding this rejection. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The rejection for limited enablement is respectfully traversed.

At the outset, Applicants and their attorneys appreciate that the previous grounds of rejection set forth in the June 25, 1996 Office Action have been relaxed with respect to 5' labeling. It is believed, however, that for the reasons given below and the attached exhibits, the instant invention is enabling for all labeling positions in a sugar moiety.

As amended, the instant invention is directed a sugar labeled nucleotide (claims 272-297 and 304-305), an oligo- or polynucleotide comprising at least one such sugar labeled nucleotide (claims 238-264, 270-271 and 306-307), a composition comprising such an oligo- or polynucleotide (claims 265-269), a composition comprising at least one such sugar labeled nucleotide (claims 299-303), and a composition comprising a polymeric compound having attached directly or indirectly thereto at least one such

sugar labeled nucleotide (claims 308-338). As noted in the latest rejection, subject matter directed to the 2', 3' and 5' positions has been deemed to be enabled. But as pointed out by Applicants in their previous December 26, 1996 Amendment (page 6, second full paragraph):

. . . the literature at the time of the invention disclosed the transformation of sugar moieties in nucleosides and nucleotides by various techniques and at various positions. By combining the prior art techniques with the teachings of the present application, one skilled in the art could certainly practice the invention at other positions . . .

It should not be overlooked, moreover, that similar if not the same chemistry can be applied to the sugar moiety at different positions. An obvious candidate for modification in any sugar moiety is the hydroxyl group usually present at each position. Other groups that are less active or even relatively inert could also be activated or functionalized and thus rendered suitable for labeling. Thus, the present invention should not be limited to the 2', 3' and 5' positions in the sugar moiety, but for all positions therein. Only by so doing can Applicants obtain a truly meaningful degree of protection for their claimed invention.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the objection and rejection under §112, first paragraph.

#### **The Rejection for Obviousness-Type Double Patenting**

Claims 238-297 and 299-338 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 5,260,433. The Examiner's remarks concerning the double patenting rejection are set forth on pages 3 and 4 of the April 15, 1997 Office Action.

In response, Applicants are submitting herewith attached as Exhibit F a Terminal Statutory Disclaimer together with a Certificate Under 37 C.F.R. §3.73(b). The attached Terminal Statutory Disclaimer (Exhibit F) specifically cites both the instant application (Serial No. 08/486,066) and the patent which is the basis for the disclaimer (U.S. Patent No. 5,260,433). In the Terminal Disclaimer signed by its undersigned attorney of record, the present assignee, Enzo Diagnostics, Inc., disclaims the terminal part of any patent granted on the instant application which would extend beyond November 9, 2010, i.e., the expiration date of U.S. Patent No. 5,260,433.

Dean L. Engelhardt et al.

Serial No. 08/486,066

Filed: June 7, 1995

Page 11 (Amendment Under 37 C.F.R. §1.115 - April 29, 1997)

Entry of the Terminal Disclaimer is respectfully urged, thereby obviating the double patenting rejection.

In light of the above arguments and submitted exhibits, Applicants respectfully request reconsideration and withdrawal of the two remaining grounds for rejections set forth in the April 15, 1997 Office Action, thereby placing all of the pending claims, 238-297 and 299-338 in allowable condition. An early indication of their allowability is respectfully sought.

\*\*\*\*\*

**SUMMARY AND CONCLUSIONS**

As amended, claims 238-297 and 299-338 are presented for further examination.

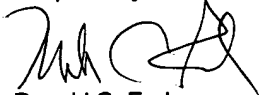
In light of the above discussion of the issues and supporting exhibits, both grounds of rejection, including 37 C.F.R. §112, first paragraph, and judicially created obviousness-type double patenting, are believed to have been overcome, thereby placing all of the pending claims, 238-297 and 299-338 in condition for allowance.

No fee is deemed necessary in connection with the filing of this amendment, other than the fee under 37 C.F.R. §1.17(r) for withdrawing the finality of the April 15, 1997 Office Action. If any other fee is deemed necessary, however, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 05-1135.

If it would be helpful to expediting prosecution of this application, Applicants' undersigned attorney may be contacted by telephone at 212-583-0100 during normal business hours.

Early and favorable action is respectfully requested.

Respectfully submitted,



Ronald C. Fedus  
Registration No. 32,567  
Attorney for Applicants

ENZO DIAGNOSTICS, INC.  
c/o Enzo Biochem, Inc.  
527 Madison Avenue (9th Floor)  
New York, New York 10022  
(212) 583-0100

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☒ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☒ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**